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April 23, 2013

Mr. Mitch Zeller
Director
ATTN: Caryn Cohen
Office of Science
Center for Tobacco Products
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

RE: Submission to the Tobacco Products Scientific Advisory Committee regarding procedures for reviewing Modified Risk Tobacco Products Applications

Dear Mr. Zeller:

Legacy appreciates the opportunity to submit comments to the Food and Drug Administration (FDA) and to the Tobacco Products Scientific Advisory Committee (TPSAC) regarding the Modified Risk Tobacco Products (MRTP) Applications (MRTPA) review process. This is perhaps one of the most important issues in the implementation of the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) and potentially a way to reduce the death and disease caused by tobacco products. However, if a robust process for pre-market approval, scrutiny of the strength of the science of the applications and meaningful post-market surveillance are not put into place, the American public health could suffer. FDA and TPSAC have a serious responsibility ahead of them.

As you know, the tobacco market has changed significantly in the past few years. New, non-combustible tobacco products are beginning to increase their share in the market, and more recently, products that do not actually contain tobacco, but rather contain tobacco-derived nicotine are being tested.

At the same time, the federal government has the opportunity to regulate cigarettes and smokeless tobacco for the first time in history; and when the FDA issues regulations asserting jurisdiction over all tobacco products, as it has indicated that it will do, it will be the first time in history that all products

containing and delivering nicotine will be regulated. Legacy urges FDA to issue its deeming regulation as soon as possible.

The topic of today's TPSAC meeting is how FDA will use the TPSAC to review Modified Risk Tobacco Product Applications. Section 911 of the Tobacco Control Act allows for the possibility that tobacco products may be developed (or may even currently exist) that present fewer health risks than combustible products, or than traditional smokeless products. We note that no tobacco product is safe, however Legacy believes that modified risk products may potentially contribute to reducing – though not eliminating – the death and disease caused by tobacco products. This is an exciting prospect, since there are millions of people who continue to be addicted to harmful tobacco products, particularly combustible tobacco products, which cause nearly one out of every two users to die prematurely.[1] However, this promise cannot be realized without proper evaluation of the products, their marketing and how they are actually used by consumers. Products should not be marketed as reduced harm unless and until strong scientific evidence proves that they will indeed reduce harm based on the actual patterns of use behavior – both to the individual and to the population as a whole, including users and non-users.

HISTORY

Legacy has submitted comments and signed on to joint comments submitted to FDA that describe in great detail the egregious practices the tobacco industry perpetrated on the American public and we incorporate by reference those details. However, the tobacco industry's long, well-documented history of making deceitful health claims about their products cannot be overstated. Most prominent are the "light" and "low tar" cigarettes that were marketed as healthier alternatives to full flavored cigarettes, though they were anything but. In a 2009 decision by the US Court of Appeals,[2] the major tobacco companies were convicted of racketeering for the fraud regarding light and low tar cigarettes. Specifically, the verdict stated:

> "As their internal documents reveal, Defendants [tobacco companies] engaged in massive, sustained, and highly sophisticated marketing and promotional campaigns to portray their light brands as less harmful than regular cigarettes." *Philip Morris*, 449 F. Supp. 2d at 860. The court concluded, "Defendants have known for decades that filtered and low tar cigarettes do not offer a meaningful reduction of risk, and that their marketing which emphasized reductions in tar and nicotine was false and misleading."[3]

Indeed, one of the functions of Section 911 is to not only make room in the market for potential tobacco products that are less harmful and could therefore reduce the toll tobacco takes on our society, but also to prevent the deception of false or misleading health claims from happening again.[4] Further, one critical lesson learned is that the impact of modified risk products must be measured directly by focusing on the behavior of actual users in real world context in representative samples and not merely by machine-measured exposures or by reliance on extrapolations from knowledge, attitudes, beliefs and risk perceptions absent directly measured behavior. It is vital when considering how to review MRTPAs that this long history remains in the minds of the TPSAC members and the FDA to serve as a reminder of the importance of this section of the Tobacco Control Act. While

some of these incidents happened more than two decades ago, individuals as well as the public are still feeling their consequences. There are still people addicted to cigarettes as a result of starting to use these products. What is worse, there are still people getting sick and dying as a result of their use of these products. Regardless of how long ago these incidents happened, FDA and TPSAC cannot ignore the past, and indeed must learn from it.

THE PUBLIC HEALTH STANDARD

Due to the unique qualities of tobacco, and the inherent harms associated with tobacco products, the Tobacco Control Act set up a new standard for approval of tobacco products – including modified risk tobacco products – referred to as the public health standard. Sections 911(g)(1)(A) and (B) of the Tobacco Control Act state that FDA cannot issue an order allowing the marketing of a product with modified risk or reduced harm claims unless it is demonstrated that the product, as actually used by consumers will "significantly reduce the harm and the risk of tobacco related disease to individual users; *and* benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products"[5] (emphasis added). The public health standard means that MRTP applicants cannot solely rely on data showing that a product reduces harm in individuals. They must also show how the presence of a product on the market would impact broader tobacco use patterns at the population level. Possible population-level effects of the introduction of MRTPs to the market include:

- Causing sufficient numbers of tobacco product users to quit using their current product entirely and switch to the new, less harmful product, in such a manner as to reduce their risk, and the degree of harmful exposure, in a significant manner that will clearly benefit individual and public health with minimal or no unintended additional harms.
- Causing tobacco product users to delay cessation of traditional tobacco products;
- Increasing tobacco product initiation, particularly among youth and other vulnerable populations that bear a disproportionate burden of the death and disease caused by tobacco;
- Encouraging poly use of tobacco products; and
- Causing those who have already quit tobacco products to relapse back to tobacco use.

To illustrate this, we present a figure of potential tobacco use transitions among current tobacco users. Combustible use is defined as use of cigarettes, cigars, pipes, little cigars/cigarillos, and hookah. Dual use is defined as the use of both combustible and noncombustible tobacco products; at the current time, noncombustible tobacco products include chewing tobacco, dip/snuff, snus, e-cigarettes, and dissolvable products. Moving from left to right over time, individuals have the opportunity to maintain their current tobacco use behavior; switch from combustible use to dual use; switch from dual use to combustible use; switch completely to noncombustible products, or quit all tobacco products. On this figure, the red lines indicate tobacco use patterns likely to maintain or increase harms, the green dotted lines indicate patterns likely to reduce harms, and the yellow line indicates the transition with the least harm (remaining a former user over time).

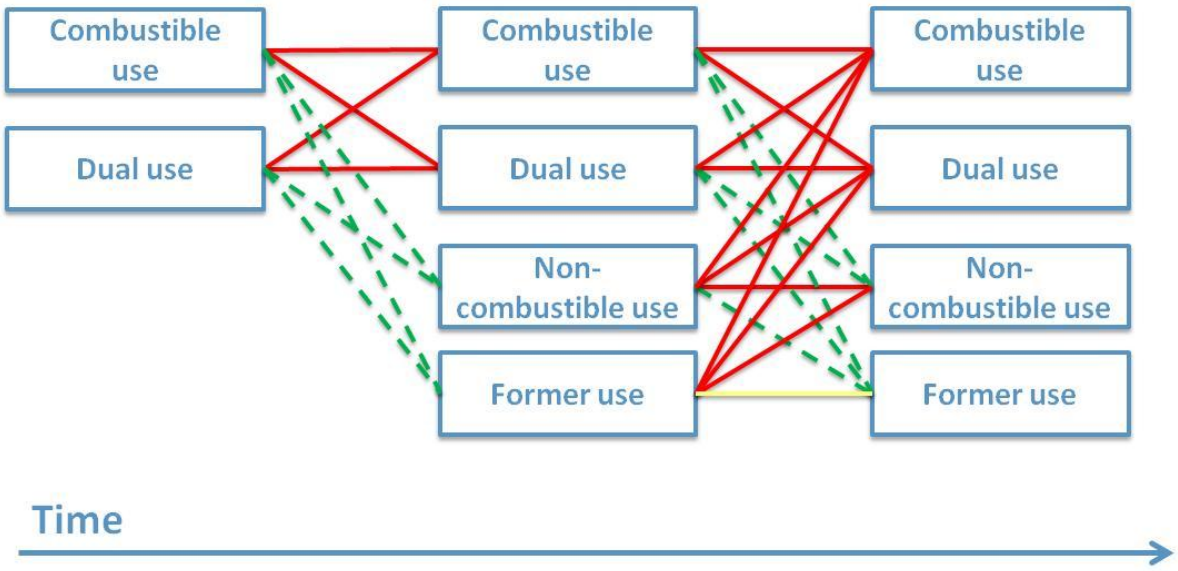

Figure 1. Possible patterns of tobacco use over time

Smokeless tobacco products are widely acknowledged to have fewer individual health risks than cigarettes or other combustible products. However, current evidence shows that smokeless tobacco products, when used in conjunction with cigarettes can have a negative impact on public health. For example, studies show that dual users of smokeless tobacco and cigarettes tend to be more likely to delay cessation of cigarette use,[6] and cigarette smoking is more prevalent among young males who use smokeless tobacco than among those who do not.[7] A longitudinal study of U.S. current tobacco users showed that the quit rate was significantly lower for cigarette smoking compared to smokeless tobacco use and that there was little switching from cigarettes to smokeless tobacco in the US (0.3% in one year).[8] Consistent with the marketing of new smokeless tobacco products encouraging dual use,[9] a study of young adult military personnel reported that initiation of smokeless tobacco use was associated with harm escalation (i.e., smoking to dual use or smokeless to smoking or dual use) rather than harm reduction (i.e., smoking to smokeless only).[10] In a nationally-representative sample of young adults conducted by researchers at Legacy, dual users of cigarettes and other tobacco products, including smokeless products, reported the same levels of smoking as cigarette-only users (8.73 vs. 9.20 cigarettes per day).[11] This finding suggests that the use of other tobacco products does not replace cigarette smoking or decrease the mean number of cigarettes smoked daily among young adults.

Therefore, if an MRTP were to promote cigarette use, or delay cessation, it would not protect public health. Similarly, because MRTPs are still not *safe*, if an MRTP appeals to youth, and encourages youth initiation of the tobacco product, this would also not protect public health. By law, the public health standard must govern decision making about modified risk product applications – FDA and TPSAC must not be distracted by data that only takes into account individual harm reduction. Otherwise, the history of the light and low tar debacle will repeat itself and millions of lives could be harmed or lost.

Legacy strongly supports the public health standard, and understands that it presents challenges in getting approval for a truly modified risk product. Nonetheless, we believe reasonable, yet rigorous pre-market requirements can be set and met that prevent fraudulent and misleading claims of modified risk, but also allow for promising products that reduce the harms caused by tobacco to enter the marketplace.

PRE-MARKET REQUIREMENTS FOR MODIFIED RISK PRODUCTS

Pre-clinical and clinical requirements

Because the public health standard is new and only applies to tobacco products, there are no direct precedents – leaving FDA to build a framework to implement the standard from scratch. However, indirect precedents do exist and important guidance has been provided to FDA by an Institute of Medicine (IOM) report on the standards to follow in order to approve an MRTP.

The Tobacco Control Act requires FDA to consult with the Institute of Medicine (IOM) in its development of guidance and regulations for approving MRTPs. The IOM Report on Scientific Standards for Studies on Modified Risk Tobacco Products[12] provides significant findings and recommendations regarding the kind of studies needed to approve an MRTPA, as well as guidance on the strength of the science needed. Legacy emphasizes the importance of these recommendations in guiding the scientific evidence needed, a phased approach to data collection and approval, the types of high quality randomized controlled trials needed to assess exposure reductions at the individual level, the delivery of high quality data, conduct of research in subpopulations of interest, good research practices, a transparent system of evidence synthesis, public disclosure of data, and proper conduct of research (Recommendations 1-9 and 11-12 of the IOM report).[i]

Additionally, while the approval standard for drugs focuses on safety and efficacy in individuals and therefore does not directly correlate to tobacco product approvals, the Investigational New Drug Application (IND) and New Drug Application (NDA) processes at FDA's Center for Drug Evaluation and Research (CDER) provide an important model for the MRTPA process.

FDA should consider designing a similar process to the Investigational New Drug Application (IND) in order to allow for testing and review of the full clinical study protocol. We note that FDA has indicated in its Guidance for Industry on Modified Risk Product Applications that it is contemplating regulations that might accomplish this.[13] We hope that FDA will issue such regulations soon, to create clear rules under which such products can be tested in humans and thereby increase the likelihood of strong, pre-market indications that a potential modified risk product actually reduces risk and meets the public health standard.

The CDER NDA process contains a phased approach for approval of a drug.[14] This means that laboratory analysis of the product and pre-clinical studies are completed before studies in humans

[i] Legacy has already provided FDA with oral testimony on our position regarding Recommendation 10 regarding third party governance of research on MRTPs, and will be submitting written testimony for the docket that has been opened on that subject. For the purposes of this meeting and submission, we will not address Recommendation 10 at this time, but refer TPSAC and FDA to our oral testimony, as well as our future written testimony.

are allowed. This is as appropriate for tobacco products as it is for drugs, as it can minimize risk to humans and prevent humans from being the guinea pigs of the tobacco industry – which was the case before the Tobacco Control Act was passed.[15,16] The IOM report also included as Recommendation 2 a phased approach to research on MRTPs.[17] This is a key element and should be explicitly included in FDA's Guidance for Industry Modified Risk Tobacco Product Applications.

Legacy recommends an extension of the phased approach to capture potential impacts at the population level, in addition to the preclinical and clinical studies needed to demonstrate reduced harm at the individual level. We propose a final phase of pre-market studies that rigorously assess actual use of the proposed MRTP; bio-markers of harm; dual use potential of the potential MRTP and conventional tobacco products; impacts on initiation and progression of tobacco use; and delay of cessation of conventional tobacco products. As the final stage of product testing, these studies will only be conducted on products that meet thresholds for reduced harm at the individual level given preclinical and clinical data. Potential mechanisms for such research would be randomized controlled trials conducted in limited test markets that have been pre-approved by FDA through the phased approach similar to CDER's IND application process. As we discuss in detail later, this would also require approval of marketing materials used in these test markets throughout the duration of the trial to reduce the likelihood of consumer deception regarding false health or reduced exposure claims.

Legacy strongly supports the IOM Report Recommendation 6[18] that requires studies and/or oversampling of vulnerable populations such as youth, ethnic minorities, and those of low-socioeconomic status – all of whom have been traditional targets of tobacco industry marketing and product development and often bear a disproportionate burden of tobacco-related disease. We encourage FDA to be more explicit in requiring testing in these populations in its Guidance to Industry. While there is a brief mention of "oversampling of populations particularly likely to be affected, positively or negatively, by the marketing of the product"[19], because of the long history of tobacco industry marketing and developing products specifically designed to attract the aforementioned populations, we believe testing in these priority populations should be required.

Legacy emphasizes IOM Report Finding and Recommendation 5 that modeling studies can provide insight into each stage of the MRTP development and approval process. That said, in order for modeling studies to be useful, the models and data used to populate the models must be scientifically valid and based on direct measures of actual patterns of use behaviors in representative samples and in relevant contexts over sufficient time frames to accurately ensure that modeling assumptions are based on real world measurements. Currently, in its Guidance for Industry on Modified Risk Tobacco Product Applications, FDA does not advocate any specific modeling system.[20] Legacy urges FDA to be more specific in its modeling requirements so that the models developed can be used across all MRTP applications and essential data collected for each MRTPA at every phase to best inform the models. This will inform the development of thresholds for results at each phase of data collection (e.g., preclinical, clinical, population study) at which a given MRTPA can move forward or be rejected. Updates to these models throughout the post-market surveillance period will also be required to determine when an approved MRTP should be removed from the market. In

addition, these models will permit simultaneous comparison of proposed MRTPs which may inform updates to requirements made by FDA for the MRTPA process.

Marketing plan, labeling and marketing material testing

As with the long-standing drug approval process, which requires approval and monitoring of marketing materials, the marketing of MRTPs is a key part of their approval process. As experienced with "light," "low tar" and "mild" cigarettes, the marketing of MRTPs is likely to have a significant influence on consumer perceptions and use of these products, including dual use of MRTPs with other traditional tobacco products. Central to the approval of MRTPAs are pre-market studies of marketing plans and materials, including advertisements and labels for potential MRTPs. The impact of marketing on actual patterns of use behavior in representative samples should be considered as an essential part of the premarket evaluation process.

As we have previously stated, one of the biggest concerns with historic, so-called modified risk products was that they were marketed falsely as healthier than other products. Therefore, factual labels, marketing plans and materials for MRTPs that do not mislead consumers will serve as a key part of MRTPAs. Any issuance of an order to market an MRTP requires not only rigorous pre-market testing of labeling, marketing and advertising materials by the MRTP applicant, but also requires rigorous scrutiny by FDA of the marketing plan, materials and studies conducted as part of an MRPTA.

Legacy has concerns in several areas with regard to the pre-market testing requirements of the marketing plans and materials. We provide four recommendations to address these concerns.

First, we reiterate our strong agreement with the IOM report that labeling, marketing plans and materials be tested in a range of populations, including vulnerable populations – particularly those that have been traditionally targeted by the tobacco industry.

Second, we recommend that MRTPAs should include pre-market studies assessing the impact of proposed marketing messages on knowledge, attitudes, perceptions, beliefs and actual tobacco use behavior. In contrast to typical marketing studies, focus group testing is insufficient in this case to assess the likely population impacts of marketing messages on initiation, cessation, and overall population harms. Rigorous trials of marketing messages pre-reviewed by FDA must be conducted to determine the effects of marketing messages on tobacco use behavior, in addition to consumer perceptions related to the proposed MRTP. Evaluation of marketing messages prior to approval of an MRTP could be conducted in conjunction with the final phase of pre-market data collection recommended above, in which studies are conducted in limited test markets to evaluate actual use behavior patterns in context over sufficient time to evaluate potential unintended consequences.

Third, consistent with public statements of the two largest U.S. tobacco companies,[21,22] we believe that MRTP marketing plans should be aligned with the goal of tobacco harm reduction. The recent acquisition of smokeless tobacco,[23] e-cigarette,[24] and pharmaceutical nicotine companies[25,26] by the largest cigarette companies in the U.S. signals the industry's commitment to rapid development and distribution of noncombustible tobacco products in the coming years.

Reports from Philip Morris International (PMI)[27] and Reynolds American[28] as well as a CTP docket submission by Altria[29] state the industry's long term, commitment to develop and promote noncombustible tobacco products. This is a clear paradigm shift, described by Philip Morris USA as an "adjacency strategy"[30] to address "the tobacco industry declining sales and…limits on the company's ability to grow cigarette revenue."[31] PMI's 2012 Investor Day highlighted several company noncombustible tobacco product initiatives including the launch of Marlboro snus; the development of technology relating to dissolvable/chewable tobacco strips, rods, and pellets; the development of "next generation products" including one that delivers nicotine aerosol via the pulmonary route;[32,33] and the development of two new factories in Europe to mass produce next generation products by 2016. Additionally, Altria launched a new company (NuMark) to release the Verve nicotine lozenge. The Reynolds American website includes a section focused on "tobacco harm reduction"[34] that details their 2006 acquisition of the American Snuff Company[35] and their 2009 purchase of Niconovum AB which develops and markets nicotine replacement products under the brand name Zonnic.[36] Reynolds American is test marketing an e-cigarette (Vuse) and smokeless pouches and pellets in select tobacco outlets,[37] moving the company toward its goal of becoming a "total tobacco company."[38] Lorillard Tobacco Company, the largest manufacturer of mentholated cigarettes in the U.S., recently purchased the manufacturer of Blu e-cigarettes.[39] In concert with these changes, the industry has urged CTP to apply a flexible standard for approving claims of modified risk tobacco product submissions to permit entry of new noncombustible tobacco products into the market.[40]

At the same time, we note that cigarettes are still the main business of the major U.S. tobacco companies. This was spelled out quite clearly by the CEO of Reynolds American, Daniel Delen at a November 2012 Call to Investors when he said, "We have a little mantra inside of the company that we use, which we call the 80-90-90. And the way that this kind of works is from a brand support expenditure, we spend about 80% of our resources in the combustible space. The combustible space is still 80%, 80-plus percent of our operating income. We spend the majority of our resources still in the combustible space. 90% of the organizational focus, the human resources inside the company, are actually focused on the combustible space. And despite a lot of these new innovations that you see coming out, 90% of our R&D budgets are actually directed at the combustible category."[41] Thus, while the companies do appear to be embracing the promise of innovative, non-combustible products, the large majority of their vast resources are still focused on cigarettes. That makes the public health standard key to ensuring that any products applying to be advertised as MRTPs actually reduce harm and are not used in conjunction with or to delay cessation of traditional cigarettes.

To that end, we believe that all MRTP marketing plans must contain consumer education about the product to improve public health, for example, promoting total switching to the reduced harm product from a traditional tobacco product. Similarly, we encourage consumer education on the fact that dual use of a modified risk product and traditional tobacco products does not improve individual or public health. This contrasts with advertising campaigns of several novel tobacco products that have been introduced in recent years that encourage dual use and promote use of the product when a user cannot smoke.

For example, early ads for Camel Snus talk about the product being "airport-friendly"[42] and "ridiculously long conference call-friendly"[43] indicating it was a product to use when you could not smoke. The ads for Marlboro Snus were even more explicit, with "Fits alongside your smokes. When smoking isn't an option, reach for Marlboro Snus."[44] More recent ads include language such as: "Smokeless for Smokers – Reach for Marlboro Snus."[45] Other product ads include an ad for blu electronic cigarettes that depict an older woman extending her middle finger to the text: "Dear Smoking Ban," followed by smaller text: "Take back your freedom to smoke anywhere with blue electronic cigarettes. Blu produces no smoke and no ash, only vapor, making it the smarter alternative to regular cigarettes. It's the most satisfying way to tell the smoking bans to kiss off. Okay, maybe the second-most satisfying way."[46] The ad suggests you can smoke electronic cigarettes when you cannot use cigarettes but makes no mention of the fact that doing so ***without*** completely stopping cigarettes could result in no reduction in harm, or even in harm escalation -- for example, dual use could result in the user delaying cessation of cigarettes because of either a misperception of harm reduction or because using the e-cigarette provides a bridge that reduces nicotine withdrawal discomfort when one cannot smoke, and reducing the motivation to quit smoking cigarettes.

We note that the products mentioned above have not received orders to be marketed as MRTPs under the law, nor are we necessarily suggesting that they should. Rather, we use them as examples of marketing of novel products that would <u>not</u> protect public health and should not be replicated for products that do receive modified risk product orders from FDA.

Finally, we urge FDA to require that ALL marketing, labeling and advertising materials for MRTPs – and not just a sampling – be reviewed and tested by FDA prior to being allowed in the marketplace, to ensure that messaging is not false or misleading. We also urge FDA to require that any changes in messaging, labeling or advertising be reviewed and tested by FDA before they are released into the marketplace. It is likely that messages about MRTPs will have to be carefully crafted to ensure consumer perceptions of the product are accurate. Any changes to messaging must be tested to prevent misunderstandings by consumers of risk and/or exposure.

We cannot overstate the importance of marketing with regard to MRTPs. We cannot allow a situation similar to the "light" and "low tar" fraud to happen again. It is in line with stated goals of several tobacco companies to provide appropriate education to consumers to reduce tobacco-related harms. The Industry must properly tune messages so that consumers understand how these products differ from traditional tobacco products and what that means for their health – both before and after a product is on the market.

POST-MARKET SURVEILLANCE

We believe that there are many kinds of reasonable pre-market studies that should be conducted prior to any issuance by FDA of an order to market a MRTP. However, we also realize that it is impossible to provide all information regarding the impact on both individual and public health before a product is actually in the marketplace. Therefore, post-market surveillance of MRTPs must be extremely robust, in order to prevent unnecessary disease and death related to use of an MRTP.

To that end, we encourage FDA to build its capacity to conduct its own post-market surveillance of MRTPs in addition to that required of the industry. FDA should build the capacity to ensure MRTP applicant compliance with approved marketing plans, labeling, and marketing messages. Further, FDA needs to ensure that it has the capacity to verify the industry studies submitted as part of an MRTPA and their post-market surveillance.

While this is not necessarily part of the application process, Legacy urges FDA to create guidance and regulations for immediate removal of products from the marketplace, should post-market surveillance show that the product or its advertising is not meeting the requirements set out by Section 911 of the Tobacco Control Act. That is, that the product as actually used does not reduce harm or that its marketing is misleading and does not protect public health. This is consistent with the drug- approval process, where there are mechanisms in place to remove drugs from the marketplace or change marketing claims should post-market surveillance show that the product is not safe and effective, or that its marketing is misleading.

The Tobacco Control Act requires annual reports from MRTP applicants who receive an order to market an MRTP. We encourage FDA to require frequent follow up assessment throughout each year that the product is on the market. Once an MRTP is on the market, actual behavior as well as consumer perception and reaction to marketing messages must be monitored frequently throughout the annual reporting period. Similarly, while some health effects – both in individuals and in the population as a whole – may take time to manifest, applicants granted an order to market an MRTP should be required to monitor them frequently. We recommend requiring baseline measurements and follow up at least as frequently as 3, 6, 9 and 12 months for each reporting period.

With regard to marketing, new media will have to also be carefully monitored once an MRTP is on the market to ensure compliance with the marketing plans as they are approved. We encourage FDA to monitor and prevent third parties from making false or misleading claims about MRTPs. Legacy's Schroeder Institute has more information on such third party advertisements and is happy to provide them to FDA and TPSAC.

As stated above, modeling studies can provide valuable information both pre- and post-market. Updates to model parameters collected via post-market surveillance will be essential to projecting the future impact of subtle changes in tobacco product use on individual and population health. Development of models and data collection to inform specific parameters at all stages of product development and marketing will be essential to maximal and meaningful use of this important tool.

TRANSPARENCY

Legacy has consistently advocated for transparency in all issues regarding the implementation of the Tobacco Control Act. The long history of fraud perpetrated by the tobacco industry has created strong distrust of the industry. To compensate for that, transparency on the part of FDA as well as the industry is necessary.

In the case of MRTPs, the statute specifically requires FDA to make MRTP applications, except for trade secrets or confidential commercial information, available to the public open to public

comment. Legacy urges FDA to create a system that makes applications available to the public as soon as possible, and that the standards for "trade secrets" and "confidential commercial information" not be overbroad, such that it is impossible to meaningfully evaluate the applications. Finally, we urge that comment periods be sufficiently long in order for interested persons to review applications and to compile substantive comments.

CONCLUSION

Legacy is hopeful of the potential that modified risk products may hold in helping to reduce the death and disease caused by tobacco. However, we also believe that strong science must prove reduced risk at both the individual and population levels before such a product can enter the marketplace. TPSAC has a difficult, but critical task in assessing the strength of the science presented in MRTPAs. Further, there is a careful balancing act that must be done by FDA in ensuring that the bar is not set too high so that truly reduced risk products are prevented from entering the market, but is high enough so that individual and public health are protected. We believe the suggestions we have made here are reasonable and achievable. We look forward to working with TPSAC and FDA on this and other issues and to continuing to protect the public health.

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